

PR 27-MAR-1998; 98US-0079751
XX

PA (USSH) US DEPT HEALTH & HUMAN SERVICES.
XX
PI Newton DL, Rybak SM;
XX
DR WPI: 1999-610847/52.
DR N-PSDB: AA208129.
XX
PT New recombinant ribonucleases, used for killing target cells, e.g. for
XX treating cancers, viral infections or autoimmune diseases
PS Claim 34; Page 61; 71pp; English.
XX
CC The present sequence is a recombinant Rana pipiens ribonuclease (RapLRI)
CC protein with Met at position 1 and GlnSer. Carboxy terminal end of
CC recombinant RapLRI has a covalently bound ligand binding moiety, which
CC can be a LL2 antibody directed against CD22 on cancerous B cells or human
CC chorionic gonadotropin (hCG) effective against Kaposi's sarcoma cells.
CC Recombinant ribonucleases can be expressed in bacteria without an N-
CC terminal methionine due to the presence of a signal peptide that is
CC cleaved by bacteria. The soluble expression of ribonuclease allows the
CC proteins to be fused in-frame with ligand binding moieties to form
CC cytotoxic fusion proteins. They can be used for treatment of cancer and
CC autoimmune diseases.
XX
SQ Sequence 105 AA;
XX
Query Match 100.0%; Score 582; DB 20; Length 105;
Best Local Similarity 100.0%; Pred. No. 1,1e-62;
Matches 105; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
XX
QY 1 MSMDLFFQKKHLNTRDVCNINIMSTNLFHCKDKNTFTYSRPPVKAICKGIASKNVLT 60
Db 1 MSMDLFFQKKHLNTRDVCNINIMSTNLFHCKDKNTFTYSRPPVKAICKGIASKNVLT 60
QY 61 TSEFYISDCNVTSRPCKYKLLKSTNFCVTCENQAPVHFEVGHGHC 105
Db 61 TSEFYISDCNVTSRPCKYKLLKSTNFCVTCENQAPVHFEVGHGHC 105
XX
RESULT 2
AAV28867
ID AAV28867 standard; Protein; 105 AA.
XX
AC AAV28867;
XX
DT 25-JAN-2000 (first entry)
XX
DE Recombinant Met(-1) RapLRI.
XX
KW Recombinant Met(-1) Rana pipiens ribonuclease; RapLRI; CD22; RNase;
KW covalently bound; LL2 antibody; ligand binding moiety; cancerous B cell;
KW Kaposi's sarcoma; human chorionic gonadotropin; hCG; signal peptide;
KW recombinant ribonuclease; cytotoxic fusion protein; cancer; frog;
XX autoimmune disease.
XX
OS Rana pipiens.
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Misc-difference 1 /note= "Met not found in wild type RapLRI"
XX
XX W09950398-A2.
XX
XX 07-OCT-1999.
XX
XX 26-MAR-1999; 99WO-US06641.
XX
XX 27-MAR-1998; 98US-0079751.
XX
XX (USSH) US DEPT HEALTH & HUMAN SERVICES.
XX
XX Newton DL, Rybak SM;
PI

XX
DR WPI: 1999-610847/52.
DR N-PSDB: AA208126.
XX
PT New recombinant ribonucleases, used for killing target cells, e.g. for
XX treating cancers, viral infections or autoimmune diseases
PS Claim 34; Page 57; 71pp; English.
XX
CC The present sequence is a recombinant Rana pipiens ribonuclease (RapLRI)
CC protein with Met at position 1. Carboxy terminal end of recombinant
CC RapLRI has a covalently bound ligand binding moiety, which can be a LL2
CC antibody directed against CD22 on cancerous B cells or human chorionic
CC gonadotropin (hCG) effective against Kaposi's sarcoma cells. Recombinant
CC ribonucleases can be expressed in bacteria without an N-terminal
CC methionine due to the presence of a signal peptide that is cleaved by
CC bacteria. The soluble expression of ribonuclease allows the proteins to
CC be fused in-frame with ligand binding moieties to form cytotoxic fusion
CC proteins. They can be used for treatment of cancer and autoimmune
CC diseases.
XX
SQ Sequence 105 AA;
XX
Query Match 99.3%; Score 578; DB 20; Length 105;
Best Local Similarity 99.0%; Pred. No. 3,4e-62;
Matches 104; Conservative 0; Mismatches 1; Indels 0; Gaps 0;
XX
QY 1 MSMDLFFQKKHLNTRDVCNINIMSTNLFHCKDKNTFTYSRPPVKAICKGIASKNVLT 60
Db 1 MSMDLFFQKKHLNTRDVCNINIMSTNLFHCKDKNTFTYSRPPVKAICKGIASKNVLT 60
QY 61 TSEFYISDCNVTSRPCKYKLLKSTNFCVTCENQAPVHFEVGHGHC 105
Db 61 TSEFYISDCNVTSRPCKYKLLKSTNFCVTCENQAPVHFEVGHGHC 105
XX
RESULT 3
AAV28870
ID AAV28870 standard; Protein; 104 AA.
XX
AC AAV28870;
XX
DT 25-JAN-2000 (first entry)
XX
DE Recombinant RapLRI GlnSer amino acid sequence.
XX
KW Recombinant Rana pipiens ribonuclease; RapLRI GlnSer; covalently bound;
KW LL2 antibody; ligand binding moiety; CD22; cancerous B cell; frog;
KW Kaposi's sarcoma; human chorionic gonadotropin; hCG; signal peptide;
KW recombinant ribonuclease; cytotoxic fusion protein; cancer; RNase;
XX autoimmune disease.
XX
OS Rana pipiens.
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Misc-difference 1 /note= "wild type Gln replaced with Ser"
XX
XX W09950398-A2.
XX
XX 07-OCT-1999.
XX
XX 26-MAR-1999; 99WO-US06641.
XX
XX 27-MAR-1998; 98US-0079751.
XX
XX (USSH) US DEPT HEALTH & HUMAN SERVICES.
XX
XX Newton DL, Rybak SM;
XX
XX WPI: 1999-610847/52.
XX
XX N-PSDB: AA208126.
DR

XX New recombinant ribonucleases, used for killing target cells, e.g. for
 PT treating cancers, viral infections or autoimmune diseases -
 XX
 PS Claim 34; Page 60; 71pp; English.

CC The present sequence is a recombinant Rana pipiens ribonuclease (RapLr1)
 CC protein with a His6 tag. Carboxy terminal end of recombinant RapLr1 has a
 CC covalently bound ligand binding moiety, which can be a IL2 antibody
 CC directed against CD22 on cancerous B cells or human chorionic
 CC gonadotropin (hCG) effective against Kaposi's sarcoma cells. Recombinant
 CC ribonucleases can be expressed in bacteria without an N-terminal
 CC methionine due to the presence of a signal peptide that is cleaved by
 CC bacteria. The soluble expression of ribonuclease allows the proteins to
 CC be fused in-frame with ligand binding moieties to form cytotoxic fusion
 CC proteins. They can be used for treatment of cancer and autoimmune
 CC diseases.

XX
 XX Sequence 104 AA;
 SQ

Query Match 99.1%; Score 577; DB 20; Length 104;
 Best Local Similarity 100.0%; Pred. No. 4.4e-62;
 Matches 104; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 2 SDMLTFQKKHLTNTRDVCNNIMSTNLFHCKDKNTFTYSRPPVKAICKGIASKNVLT 61
 DB 1 SDMLTFQKKHLTNTRDVCNNIMSTNLFHCKDKNTFTYSRPPVKAICKGIASKNVLT 60
 OY 62 TSEFYLSDCNVTSPCKKYKLLKSTNTFCVTCENQAPVHFGVGHG 105
 DB 61 TSEFYLSDCNVTSPCKKYKLLKSTNTFCVTCENQAPVHFGVGHG 104

RESULT 4
 AAY28869
 ID AAY28869 standard; Protein: 105 AA.
 AC AAY28869;
 XX
 DT 25-JAN-2000 (first entry)
 XX
 DE Recombinant Met(-3) RapLr1 Met23Leu-(His)6 protein.
 XX
 KW Recombinant Met(-1) Rana pipiens ribonuclease Met23Leu-(His)6; RapLr1;
 KW CD22; covalently bound; IL2 antibody; ligand binding moiety; RNase;
 KW cancerous B cell; Kaposi's sarcoma; human chorionic gonadotropin; hCG;
 KW signal peptide; recombinant ribonuclease; cytotoxic fusion protein;
 KW cancer; frog; autoimmune disease.
 XX
 OS Rana pipiens.
 OS Synthetic.
 OS
 FT Key Location/Qualifiers
 FT Misc-difference 1 /note- "(His)6 histidine tag attached to N-terminal Met"
 FT Misc-difference 1 /note- "Met not found in wild type RapLr1"
 FT Misc-difference 24 /note- "Wild type Met replaced with Leu"
 FT
 PN WO950398-A2.
 PD 07-OCT-1999.
 PF 26-MAR-1999; 99WO-US06641.
 PR 27-MAR-1998; 98US-0079751.
 PA (USSH) US DEPT HEALTH & HUMAN SERVICES.
 PS Newton DL, Rybak SM;
 WPI: 1999-610847/52.

DR N-PSDB; AA208127.
 XX
 PT New recombinant ribonucleases, used for killing target cells, e.g. for
 PT treating cancers, viral infections or autoimmune diseases -
 XX
 PS Claim 4; Page 59; 71pp; English.

CC The present sequence is a recombinant Rana pipiens ribonuclease protein
 CC (RapLr1) with Met at position 1 attached to (His)6 tag and Met24Leu.
 CC Carboxy terminal end of recombinant RapLr1 has a covalently bound ligand
 CC binding moiety, which can be a IL2 antibody directed against CD22 on
 CC cancerous B cells or human chorionic gonadotropin (hCG) effective
 CC against Kaposi's sarcoma cells. Recombinant ribonucleases can be
 CC expressed in bacteria without an N-terminal methionine due to the
 CC presence of a signal peptide that is cleaved by bacteria. The soluble
 CC expression of ribonuclease allows the proteins to be fused in-frame with
 CC ligand binding moieties to form cytotoxic fusion proteins. They can be
 CC used for treatment of cancer and autoimmune diseases.

XX
 XX Sequence 105 AA;
 SQ

Query Match 98.8%; Score 575; DB 20; Length 105;
 Best Local Similarity 98.1%; Pred. No. 7.8e-62;
 Matches 103; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

OY 1 MSDMLTFQKKHLTNTRDVCNNIMSTNLFHCKDKNTFTYSRPPVKAICKGIASKNVLT 60
 DB 1 MSDMLTFQKKHLTNTRDVCNNIMSTNLFHCKDKNTFTYSRPPVKAICKGIASKNVLT 60
 OY 61 TSEFYLSDCNVTSPCKKYKLLKSTNTFCVTCENQAPVHFGVGHG 105
 DB 61 TSEFYLSDCNVTSPCKKYKLLKSTNTFCVTCENQAPVHFGVGHG 105

RESULT 5
 AAY28865
 ID AAY28865 standard; Protein: 104 AA.
 AC AAY28865;
 XX
 DT 25-JAN-2000 (first entry)
 XX
 DE Rana pipiens liver ribonuclease (RapLr1).
 XX
 KW Rana pipiens liver ribonuclease; RapLr1; covalently bound; IL2 antibody;
 KW ligand binding moiety; CD22; cancerous B cell; Kaposi's Sarcoma; frog;
 KW human chorionic gonadotropin; hCG; recombinant ribonuclease; RNase;
 KW signal peptide; cytotoxic fusion protein; cancer; autoimmune disease.
 XX
 OS Rana pipiens.
 OS
 FT Key Location/Qualifiers
 FT Misc-difference 1 /note- "(His)6 histidine tag attached to N-terminal Met"
 FT Misc-difference 1 /note- "Met not found in wild type RapLr1"
 FT Misc-difference 24 /note- "Wild type Met replaced with Leu"
 FT
 PN WO950398-A2.
 PD 07-OCT-1999.
 PF 26-MAR-1999; 99WO-US06641.
 PR 27-MAR-1998; 98US-0079751.
 PA (USSH) US DEPT HEALTH & HUMAN SERVICES.
 PS Newton DL, Rybak SM;
 WPI: 1999-610847/52.
 DR N-PSDB; AA208124.
 XX
 PT New recombinant ribonucleases, used for killing target cells, e.g. for
 PT treating cancers, viral infections or autoimmune diseases -
 XX
 PS Claim 1; Page 55; 71pp; English.

CC The present sequence is Rana pipiens liver ribonuclease (RapLr1)
 CC protein. Carboxy terminal end of RapLr1 has a covalently bound

CC ligand binding moiety, which can be a LL2 antibody directed against
 CC CD22 on cancerous B cells or human chorionic gonadotropin (hCG)
 CC effective against Kaposi's sarcoma cells. Recombinant ribonucleases can
 CC be expressed in bacteria without an N-terminal methionine due to the
 CC presence of a signal peptide that is cleaved by bacteria. The soluble
 CC expression of a ribonuclease allows the proteins to be fused in-frame with
 CC ligand binding moieties to form cytotoxic fusion proteins. They can be
 CC used for treatment of cancer and autoimmune diseases.
 XX
 SQ Sequence 104 AA;

Query Match 98.5%; Score 573; DB 20; Length 104;
 Best Local Similarity 100.0%; Pred. No. 1.4e-61;
 Matches 103; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 3 DWLTFQKHLLTNTRDVCNNIMSTNLFHCKDKNTFTYSRPPVKAICKGIASKNVLTTS 62
 DB 2 DWLTFQKHLLTNTRDVCNNIMSTNLFHCKDKNTFTYSRPPVKAICKGIASKNVLTTS 61
 OY 63 EFTLSDCNVTSRPPCKYKLLKSTNTFCVTCENQAPVHFVGVC 105
 DB 62 EFTLSDCNVTSRPPCKYKLLKSTNTFCVTCENQAPVHFVGVC 104

RESULT 6

AAI288679 standard; Protein; 127 AA.

AAI28879;

25-JAN-2000 (first entry)

Rana pipiens Clone 5a1b ribonuclease.

Rana pipiens ribonuclease Clone 5a1b; RAPIR1; covalently bound; RNase;
 LL2 antibody; ligand binding moiety; CD22; cancerous B cell; onconase;
 Kaposi's sarcoma; human chorionic gonadotropin; hCG; cancer;
 recombinant ribonuclease; frog; signal peptide; cytotoxic fusion protein;
 autoimmune disease.

Rana pipiens.

Key Location/Qualifiers
 1..23
 /Label= Signal-peptide
 /note= "Putative"
 24..127
 /Label= Rana_pipiens_Clone_5a1b_ribonuclease

WO9950398-A2.

07-OCT-1999.

26-MAR-1999; 99WO-US06641.

27-MAR-1998; 98US-0079751.

(USSH) US DEPT HEALTH & HUMAN SERVICES.

Newton DL, Rybak SM;

WPI: 1999-610847/52.

N-PSDB: AA208136.

New recombinant ribonucleases, used for killing target cells, e.g. for
 treating cancers, viral infections or autoimmune diseases -

Disclosure: Page 69; 71pp; English.

The present sequence is a Rana pipiens Clone 5a1b ribonuclease (RAPIR1).
 It is encoded by Clone 5a1b cDNA obtained from Rana pipiens liver mRNA
 library. It exhibits differences with Onconase (RTM) at amino acid
 residues 11, 20, 85 and 103. Carboxy terminal end of RAPIR1 has a

CC covalently bound ligand binding moiety, which can be a LL2 antibody
 CC directed against CD22 on cancerous B cells or human chorionic
 CC gonadotropin (hCG) effective against Kaposi's Sarcoma cells. Recombinant
 CC ribonucleases can be expressed in bacteria without an N-terminal
 CC methionine due to the presence of a signal peptide that is cleaved by
 CC bacteria. The soluble expression of ribonuclease allows the proteins to
 CC be fused in-frame with ligand binding moieties to form cytotoxic fusion
 CC proteins. They can be used for treatment of cancer and autoimmune
 CC diseases.
 XX
 SQ Sequence 127 AA;

Query Match 98.5%; Score 573; DB 20; Length 127;
 Best Local Similarity 100.0%; Pred. No. 1.7e-61;
 Matches 103; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 3 DWLTFQKHLLTNTRDVCNNIMSTNLFHCKDKNTFTYSRPPVKAICKGIASKNVLTTS 62
 DB 25 DWLTFQKHLLTNTRDVCNNIMSTNLFHCKDKNTFTYSRPPVKAICKGIASKNVLTTS 84
 OY 63 EFTLSDCNVTSRPPCKYKLLKSTNTFCVTCENQAPVHFVGVC 105
 DB 85 EFTLSDCNVTSRPPCKYKLLKSTNTFCVTCENQAPVHFVGVC 127

RESULT 7

AAI28866 standard; Protein; 104 AA.

AAI28866;

25-JAN-2000 (first entry)

Recombinant RAPIR1 Met23Leu amino acid sequence.

Recombinant Rana pipiens ribonuclease; RAPIR1 Met23Leu; covalently bound;
 LL2 antibody; ligand binding moiety; CD22; cancerous B cell; RNase;
 Kaposi's sarcoma; human chorionic gonadotropin; hCG; signal peptide;
 recombinant ribonuclease; cytotoxic fusion protein; cancer; frog;
 autoimmune disease.

Rana pipiens.
 Synthetic.

Key Location/Qualifiers
 23
 /note= "Wild type Met replaced with Leu"

WO9950398-A2.

07-OCT-1999.

26-MAR-1999; 99WO-US06641.

27-MAR-1998; 98US-0079751.

(USSH) US DEPT HEALTH & HUMAN SERVICES.

Newton DL, Rybak SM;

WPI: 1999-610847/52.

N-PSDB: AA208125.

New recombinant ribonucleases, used for killing target cells, e.g. for
 treating cancers, viral infections or autoimmune diseases -

Claim 34; Page 56; 71pp; English.

The present sequence is a recombinant Rana pipiens ribonuclease (RAPIR1)
 protein with Met23Leu. Carboxy terminal end of recombinant RAPIR1 has a
 covalently bound ligand binding moiety, which can be a LL2 antibody
 directed against CD22 on cancerous B cells or human chorionic
 gonadotropin (hCG) effective against Kaposi's sarcoma cells. Recombinant

CC ribonucleases can be expressed in bacteria without an N-terminal
CC methionine due to the presence of a signal peptide that is cleaved by
CC bacteria. The soluble expression of ribonuclease allows the proteins to
CC be fused in-frame with ligand binding moieties to form cytotoxic fusion
CC proteins. They can be used for treatment of cancer and autoimmune
CC diseases.

XX Sequence 104 AA;

Query Match 97.9%; Score 570; DB 20; Length 104;
Best Local Similarity 99.0%; Pred. No. 3,1e-61;
Matches 102; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

OY 3 DMLEFQKKHITNTRDVDCNNIMSTNLFHCKDKNTFIYSRPEPVKATCGIASKNVLTTS 62

DB 2 DMLEFQKKHITNTRDVDCNNIMSTNLFHCKDKNTFIYSRPEPVKATCGIASKNVLTTS 61

OY 63 EFTLSDCNVTSRPPCKYKLRKSTNFCVTCENQAPVHFVGSHC 105

DB 62 EFTLSDCNVTSRPPCKYKLRKSTNFCVTCENQAPVHFVGSHC 104

RESULT 8

AAW35118 ID AAW35118 standard; Protein; 112 AA.

XX AAW35118;

DT 20-APR-1998 (first entry)

DE R. pipiens recombinant RNase protein NISMetSerronc

XX RNase A; ribonuclease; cytotoxic; onconase; nonc; immunofusion;

KM tumour cell growth; frog.

XX Rana pipiens.

PN W09731116-A2.

PD 28-AUG-1997.

PF 19-FEB-1997; 97MO-US02588.

PR 21-FEB-1996; 96US-0011800.

PA (USSH) US DEPT HEALTH & HUMAN SERVICES.

PI Boque L, Newton DL, Rybak SM, Wlodawer A;

DR WPI: 1997-435168/40.

DR N-PSDB; AAT949355.

XX Ribonuclease molecules based on native Onconase - used for killing

PT cells, particularly tumour cells

XX Claim 18; Page 63; 90pp; English.

CC AAW35115 to AAW35123 encode recombinant proteins (rnc) which are
CC modifications of the RNase Onconase (rnc). Such novel
CC ribonuclease molecules are highly cytotoxic and can be used alone or to
CC form chemical conjugates or to target recombinant immunofusions. They are
CC used particularly for decreasing tumour cell growth. They can also be
CC used for cell separation in vitro by selectively killing unwanted types
CC of cells, e.g. in bone marrow prior to transplantation into a patient
CC undergoing marrow ablation by radiation, or for killing leukaemia cells
CC or T-cells that would cause graft versus host disease. The toxins can
CC also be used to selectively kill unwanted cells in culture. The new
CC ribonucleases have increased cytotoxic activity compared to nonc and also
CC lower immunogenicity in humans.

XX Sequence 112 AA;

Query Match 96.2%; Score 560; DB 18; Length 112;

Best Local Similarity 96.2%; Pred. No. 5.6e-60;
Matches 101; Conservative 2; Mismatches 2; Indels 0; Gaps 0;

OY 1 MSDMLFQKKHITNTRDVDCNNIMSTNLFHCKDKNTFIYSRPEPVKATCGIASKNVLT 60

DB 8 MSDMLFQKKHITNTRDVDCNNIMSTNLFHCKDKNTFIYSRPEPVKATCGIASKNVLT 67

OY 61 TSEFTLSDCNVTSRPPCKYKLRKSTNFCVTCENQAPVHFVGSHC 105

DB 68 TSEFTLSDCNVTSRPPCKYKLRKSTNFCVTCENQAPVHFVGSHC 112

RESULT 9

AAW35134 ID AAW35134 standard; Protein; 251 AA.

XX AAW35134;

DT 20-APR-1998 (first entry)

DE R. pipiens recombinant RNase rnc fusion protein 10.

XX RNase A; ribonuclease; cytotoxic; onconase; nonc; immunofusion;

KM tumour cell growth; frog.

XX Rana pipiens.

OS Synthetic.

PN W09731116-A2.

PD 28-AUG-1997.

PF 19-FEB-1997; 97MO-US02588.

PR 21-FEB-1996; 96US-0011800.

PA (USSH) US DEPT HEALTH & HUMAN SERVICES.

PI Boque L, Newton DL, Rybak SM, Wlodawer A;

DR WPI: 1997-435168/40.

DR N-PSDB; AAT94972.

XX Ribonuclease molecules based on native Onconase - used for killing

PT cells, particularly tumour cells

XX Disclosure; Page 76; 90pp; English.

CC Sequences AAW35125 to AAW35135 represent recombinant fusion proteins
CC (rnc) which are modifications of the RNase Onconase (rnc). Such
CC novel ribonuclease molecules are highly cytotoxic and can be used alone
CC or to form chemical conjugates or to target recombinant immunofusions.
CC They are used particularly for decreasing tumour cell growth. They can
CC also be used for cell separation in vitro by selectively killing unwanted
CC types of cells, e.g. in bone marrow prior to transplantation into a
CC patient undergoing marrow ablation by radiation, or for killing leukaemia
CC cells or T-cells that would cause graft versus host disease. The toxins
CC can also be used to selectively kill unwanted cells in culture. The new
CC ribonucleases have increased cytotoxic activity compared to nonc and
CC also lower immunogenicity in humans.

XX Sequence 251 AA;

Query Match 96.2%; Score 560; DB 18; Length 251;
Best Local Similarity 96.2%; Pred. No. 1.6e-59;
Matches 101; Conservative 2; Mismatches 2; Indels 0; Gaps 0;

OY 1 MSDMLFQKKHITNTRDVDCNNIMSTNLFHCKDKNTFIYSRPEPVKATCGIASKNVLT 60

DB 147 MSDMLFQKKHITNTRDVDCNNIMSTNLFHCKDKNTFIYSRPEPVKATCGIASKNVLT 206

OY 61 TSEFTLSDCNVTSRPPCKYKLRKSTNFCVTCENQAPVHFVGSHC 105

XX

Db 207 TSEFYLSDCNVTSRPCKYKLLKSTNKFVTCENQAPVHFVGVGSC 251

RESULT 10

AAW35135
ID AAW35135 standard; Protein: 254 AA.

XX AAW35135;

XX 20-APR-1998 (first entry)

DE R. pipiens recombinant RNase ronc fusion protein 11.

KW RNase A; ribonuclease; cytotoxic; onconase; nonc; immunofusion;
tumour cell growth; frog.

OS Rana pipiens.
OS Synthetic.

PN W09731116-A2.

XX 28-AUG-1997.

PF 19-FEB-1997; 97WO-US02588.

PR 21-FEB-1996; 96US-0011800.

XX (USSH) US DEPT HEALTH & HUMAN SERVICES.

PI Boque L, Newton DL, Rybak SM, Wlodawer A;

DR WPI: 1997-435168/40.

DR N-PSDB; AAT94973.

PT Ribonuclease molecules based on native Onconase - used for killing
cells, particularly tumour cells

PS Disclosure: Page 77; 90pp; English.

Sequences AAW35125 to AAW35135 represent recombinant fusion proteins (ronc) which are modifications of the RNase Onconase (RTM) (nonc). Such novel ribonuclease molecules are highly cytotoxic and can be used alone or to form chemical conjugates or to target recombinant immunofusions. They are used particularly for decreasing tumour cell growth. They can also be used for cell separation in vitro by selectively killing unwanted types of cells, e.g. in bone marrow prior to transplantation into a patient undergoing marrow ablation by radiation, or for killing leukaemia cells or T-cells that would cause graft versus host disease. The toxins can also be used to selectively kill unwanted cells in culture. The new ribonucleases have increased cytotoxic activity compared to nonc and also lower immunogenicity in humans.

XX Sequence 254 AA;

Query Match 96.2%; Score 560; DB 18; Length 254;

Best Local Similarity 96.2%; Pred. No. 1.6e-59;

Matches 101; Conservative 2; Mismatches 2; Indels 0; Gaps 0;

OY 1 MSDMLTFOKKHILTMTRDVCNNIMSTNLFHCKDKNTFIYSRPEPVKAICKIISKVLT 60

DB 1 MSDMLTFOKKHILTMTRDVCNNIMSTNLFHCKDKNTFIYSRPEPVKAICKIISKVLT 60

OY 61 TSEFYLSDCNVTSRPCKYKLLKSTNKFVTCENQAPVHFVGVGHC 105

DB 61 TSEFYLSDCNVTSRPCKYKLLKSTNKFVTCENQAPVHFVGVGSC 105

RESULT 11

AAW35129
ID AAW35129 standard; Protein: 355 AA.

XX AAW35129;

DT 20-APR-1998 (first entry)

XX R. pipiens recombinant RNase ronc fusion protein 5.

DE RNase A; ribonuclease; cytotoxic; onconase; nonc; immunofusion;
tumour cell growth; frog.

OS Rana pipiens.
OS Synthetic.

PN W09731116-A2.

XX 28-AUG-1997.

PF 19-FEB-1997; 97WO-US02588.

PR 21-FEB-1996; 96US-0011800.

XX (USSH) US DEPT HEALTH & HUMAN SERVICES.

PI Boque L, Newton DL, Rybak SM, Wlodawer A;

DR WPI: 1997-435168/40.

DR N-PSDB; AAT94967.

PT Ribonuclease molecules based on native Onconase - used for killing
cells, particularly tumour cells

PS Disclosure: Page 71; 90pp; English.

Sequences AAW35125 to AAW35135 represent recombinant fusion proteins (ronc) which are modifications of the RNase Onconase (RTM) (nonc). Such novel ribonuclease molecules are highly cytotoxic and can be used alone or to form chemical conjugates or to target recombinant immunofusions. They are used particularly for decreasing tumour cell growth. They can also be used for cell separation in vitro by selectively killing unwanted types of cells, e.g. in bone marrow prior to transplantation into a patient undergoing marrow ablation by radiation, or for killing leukaemia cells or T-cells that would cause graft versus host disease. The toxins can also be used to selectively kill unwanted cells in culture. The new ribonucleases have increased cytotoxic activity compared to nonc and also lower immunogenicity in humans.

XX Sequence 355 AA;

Query Match 96.2%; Score 560; DB 18; Length 355;

Best Local Similarity 96.2%; Pred. No. 2.5e-59;

Matches 101; Conservative 2; Mismatches 2; Indels 0; Gaps 0;

OY 1 MSDMLTFOKKHILTMTRDVCNNIMSTNLFHCKDKNTFIYSRPEPVKAICKIISKVLT 60

DB 251 MSDMLTFOKKHILTMTRDVCNNIMSTNLFHCKDKNTFIYSRPEPVKAICKIISKVLT 310

OY 61 TSEFYLSDCNVTSRPCKYKLLKSTNKFVTCENQAPVHFVGVGHC 105

DB 311 TSEFYLSDCNVTSRPCKYKLLKSTNKFVTCENQAPVHFVGVGSC 355

RESULT 12

AAW35133
ID AAW35133 standard; Protein: 355 AA.

XX AAW35133;

XX 20-APR-1998 (first entry)

DE R. pipiens recombinant RNase ronc fusion protein 9.

KW RNase A; ribonuclease; cytotoxic; onconase; nonc; immunofusion;
tumour cell growth; frog.

OS Rana pipiens.
OS Synthetic.

XX MO9731116-A2.
XX 28-AUG-1997.
XX 19-FEB-1997; 97WO-US02588.
XX 21-FEB-1996; 96US-0011800.
XX (USSH) US DEPT HEALTH & HUMAN SERVICES.
XX Boque L, Newton DL, Rybak SK, Wlodawer A;
XX WPI; 1997-435168/40.
XX N-PSDB; AAT94971.
XX Ribonuclease molecules based on native Onconase - used for killing
XX cells, particularly tumour cells.
XX
XX Disclosure; Page 75; 90pp; English.
XX
XX Sequences AAW35125 to AAW35135 represent recombinant fusion proteins
XX (rOnc) which are modifications of the RNase Onconase (RM) (nOnc). Such
XX novel ribonuclease molecules are highly cytotoxic and can be used alone
XX or to form chemical conjugates or to target recombinant immunofusions.
XX They are used particularly for decreasing tumour cell growth. They can
XX also be used for cell separation in vitro by selectively killing unwanted
XX types of cells, e.g. in bone marrow prior to transplantation into a
XX patient undergoing marrow ablation by radiation, or for killing leukaemia
XX cells or T-cells that would cause graft versus host disease. The toxins
XX can also be used to selectively kill unwanted cells in culture. The new
XX ribonucleases have increased cytotoxic activity compared to nOnc and
XX also lower immunogenicity in humans.
XX
SQ Sequence 355 AA;
Query Match 96.2%; Score 560; DB 18; Length 355;
Best Local Similarity 96.2%; Pred. No. 2.5e-59;
Matches 101; Conservative 2; Mismatches 2; Indels 0; Gaps 0;
OY 1 MSDFLTFQKKHILNTRVDCNNIMSTNLFHCKDKNFTYSRPPVKAICKGIASKNVLT 60
DB 1 MSDFLTFQKKHILNTRVDCNNIMSTNLFHCKDKNFTYSRPPVKAICKGIASKNVLT 60
OY 61 TSEFYLSDCNVTSPCKYKRLKSTNFCVCENAPVHFVGHC 105
DB 61 TSEFYLSDCNVTSPCKYKRLKSTNFCVCENAPVHFVGHC 105
RESULT 13
AAW35132
ID AAW35132 standard; Protein: 366 AA.
XX
XX AAW35132;
XX
XX 20-APR-1998 (first entry)
XX
XX R. pipiens recombinant RNase rOnc fusion protein 8.
XX
XX RNase A; ribonuclease; cytotoxic; onconase; nOnc; immunofusion;
XX tumour cell growth; frog.
XX
XX Rana pipiens.
XX OS Synthetic.
XX
XX WO9731116-A2.
XX
XX 28-AUG-1997.
XX
XX 19-FEB-1997; 97WO-US02588.
XX
XX 21-FEB-1996; 96US-0011800.
XX

PA (USSH) US DEPT HEALTH & HUMAN SERVICES.
XX
XX Boque L, Newton DL, Rybak SM, Wlodawer A;
XX WPI; 1997-435168/40.
XX N-PSDB; AAT94970.
XX Ribonuclease molecules based on native Onconase - used for killing
XX cells, particularly tumour cells
XX
XX Disclosure; Page 74; 90pp; English.
XX
XX Sequences AAW35125 to AAW35135 represent recombinant fusion proteins
XX (rOnc) which are modifications of the RNase Onconase (RM) (nOnc). Such
XX novel ribonuclease molecules are highly cytotoxic and can be used alone
XX or to form chemical conjugates or to target recombinant immunofusions.
XX They are used particularly for decreasing tumour cell growth. They can
XX also be used for cell separation in vitro by selectively killing unwanted
XX types of cells, e.g. in bone marrow prior to transplantation into a
XX patient undergoing marrow ablation by radiation, or for killing leukaemia
XX cells or T-cells that would cause graft versus host disease. The toxins
XX can also be used to selectively kill unwanted cells in culture. The new
XX ribonucleases have increased cytotoxic activity compared to nOnc and
XX also lower immunogenicity in humans.
XX
SQ Sequence 366 AA;
Query Match 96.2%; Score 560; DB 18; Length 366;
Best Local Similarity 96.2%; Pred. No. 2.6e-59;
Matches 101; Conservative 2; Mismatches 2; Indels 0; Gaps 0;
OY 1 MSDFLTFQKKHILNTRVDCNNIMSTNLFHCKDKNFTYSRPPVKAICKGIASKNVLT 60
DB 262 MSDFLTFQKKHILNTRVDCNNIMSTNLFHCKDKNFTYSRPPVKAICKGIASKNVLT 321
OY 61 TSEFYLSDCNVTSPCKYKRLKSTNFCVCENAPVHFVGHC 105
DB 322 TSEFYLSDCNVTSPCKYKRLKSTNFCVCENAPVHFVGHC 366
RESULT 14
AAW06544
ID AAW06544 standard; Protein: 104 AA.
XX
XX AAW06544;
XX
XX 22-AUG-1997 (first entry)
XX
XX Antitumour protein from Rana pipiens oocytes.
XX
XX Tumour; chemotherapy; radiotherapy; frog.
XX
XX Rana pipiens.
XX OS
XX WO9639428-A1.
XX
XX 12-DEC-1996.
XX
XX 03-JUN-1996; 96WO-US08304.
XX
XX 06-JUN-1995; 95US-0467955.
XX
XX (ALFA-) ALFACELL CORP.
XX
XX Ardelt WJ;
XX
XX WPI; 1997-043063/04.
XX
XX Antitumour proteins from Rana pipiens oocyte(s) - have fewer
XX disadvantages than chemotherapy, surgery and radiotherapy
XX
XX Claim 8; Page 28; 45pp; English.
XX

CC The present sequence is a specifically claimed example of an
CC antitumour protein from the generic protein in AAW18224, with the
CC molecular weight 12000. This is one of two preferred proteins (the
CC other in AAW05543) that have been isolated from Rana pipiens oocytes.
CC Both proteins have a blocked amino terminal group and are essentially
CC free of carbohydrates. The proteins are used to treat tumours. Use of
CC the peptides has fewer disadvantages than chemotherapy, radiotherapy
CC and surgery in the treatment of tumours.
XX

Sequence 104 AA;

Query Match 95.5%; Score 556; DB 18; Length 104;
Best Local Similarity 97.1%; Pred. No. 1.6e-59;
Matches 100; Conservative 1; Mismatches 2; Indels 0; Gaps 0;

Oy 3 DWLTFQKKHLTNTRDVCNNIMSTNLFHCKDKNTFIYSRPPVKAICKGIASKNVLT 62
Db 2 DWLTFQKKHVTNTRDVCNNIMSTNLFHCKDKNTFIYSRPPVKAICKGIASKNVLT 61
Oy 63 EFYLSDCNVTSRPCKRYKLRKSTNTFCVTCENQAPVHFVGVC 105
Db 62 EFYLSDCNVTSRPCKRYKLRKSTNTFCVTCENQAPVHFVGVC 104

RESULT 15

AAW35123 standard; Protein: 105 AA.
AAW35123;
AC AAW35123;
XX

DT 20-APR-1998 (first entry)
XX

DE R. pipiens recombinant RNase protein [Met-(-1)]rOnc.
XX

KM RNase A; ribonuclease; cytotoxic; onconase; nOnc; immunofusion;
XX tumour cell growth; frog.

OS Rana pipiens.
XX

PN MO9731116-A2.
XX

PD 28-AUG-1997.
XX

PF 19-FEB-1997; 97WO-US02588.
XX

PR 21-FEB-1996; 96US-0011800.
XX

PA (USSH) US DEPT HEALTH & HUMAN SERVICES.
XX

PI Bogue L, Newton DL, Rybak SM, Wlodawer A;
XX

DR WPI: 1997-435168/40.
XX

DR N-PSDB: AAT94959.
XX

PT Ribonuclease molecules based on native Onconase - used for killing
XX cells, particularly tumour cells

PS Disclosure: Pages 65-66; 90pp; English.
XX

CC AAW35115 to AAW35123 encode recombinant proteins (rOnc) which are
CC modifications of the RNase Onconase (RTM) (nOnc). Such novel
CC ribonuclease molecules are highly cytotoxic and can be used alone or to
CC form chemical conjugates or to target recombinant immunofusions. They are
CC used particularly for decreasing tumour cell growth. They can also be
CC used for cell separation in vitro by selectively killing unwanted types
CC of cells, e.g. in bone marrow prior to transplantation into a patient
CC undergoing marrow ablation by radiation, or for killing leukaemia cells
CC or T-cells that would cause graft versus host disease. The toxins can
CC also be used to selectively kill unwanted cells in culture. The new
CC ribonucleases have increased cytotoxic activity compared to nOnc and also
CC lower immunogenicity in humans.
XX
SQ Sequence 105 AA;

Query Match 95.5%; Score 556; DB 18; Length 105;
Best Local Similarity 95.2%; Pred. No. 1.6e-59;
Matches 100; Conservative 2; Mismatches 3; Indels 0; Gaps 0;

Oy 1 MSDWLTQKKHLTNTRDVCNNIMSTNLFHCKDKNTFIYSRPPVKAICKGIASKNVLT 60
Db 1 MEDWLTQKKHVTNTRDVCNNIMSTNLFHCKDKNTFIYSRPPVKAICKGIASKNVLT 60
Oy 61 TSEFYLSDCNVTSRPCKRYKLRKSTNTFCVTCENQAPVHFVGVC 105
Db 61 TSEFYLSDCNVTSRPCKRYKLRKSTNTFCVTCENQAPVHFVGVC 105

Search completed: June 25, 2003, 14:48:39
Job time : 32.5 secs